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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,964	04/11/2002	Bruce M. Paterson	11613.33USWO	6025

45074 7590 04/21/2005

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,964	PATERSON ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *6-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☒ Claim(s) *1-5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0702*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election, with traverse, of Invention I, Claims 1-5, and the sequence Tyr-Ser-Gly-Pro-Pro-Ser-Gly-Ala-Arg-Arg-Arg-Asn-Cys-Tyr-Glu in their response of February 3, 2005 is acknowledged. The traversal is on the ground(s) that no undue burden would be imposed by examination of all the claims.

This is not found persuasive. The MPEP states: "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP 808.02" (see MPEP 803). The reasons searching more than one of Inventions I-IV and (A)-(F) would be a burden on the Office were clearly explained in the prior action. The Examiner cannot reply to any specific reasons why Applicants think that there is a lack of a serious burden, as reasons have not been presented. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-9 are pending. Claims 6-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-5 are examined on their merits.

Specification-Objections

The specification is objected to for not disclosing the specific sequence of the chicken myoD or the CDK4 used in the Working Examples. For purposes of examination, it is assumed that the chicken myoD used has the sequence set forth by NCBI Accession Number AAA74374, as taught by Dechesne et al, 1994.

Claims-Objections

Claims 1-5 are objected to for failing to recite a sequence identifier number for the elected sequence, Tyr-Ser-Gly-Pro-Pro-Ser-Gly-Ala-Arg-Arg-Arg-Asn-Cys-Tyr-Glu. Any sequence of more than four residues must be identified by a sequence identifier number (SEQ ID NO: _) and disclosed in the Sequence Listing. Correction is required.

Examiner's note: As per the telephonic interview with the Applicant's representative, Mark Deffner, on February 22, 2005, residues 1-15 of SEQ ID NO: 3 has the elected sequence Tyr-Ser-Gly-Pro-Pro-Ser-Gly-Ala-Arg-Arg-Arg-Asn-Cys-Tyr-Glu. Thus, the sequence of residues 1-15 of SEQ ID NO: 3 was used to search the elected invention.

Claims 1-5 are objected to for reciting non-elected subject matter.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "CDK-4 binding peptide" in Claims 1-3 and 5 renders said claims indefinite because "CDK-4" is indefinite. The definition for the phrase "CDK-4 binding peptide" on page 4, line 24, of the specification fails to define the function of a "CDK-4 binding peptide" because the specification fails to define the structure of the CDK-4 proteins that bind said "CDK-4 binding peptide". The specification, page 1, lines 12-14, defines CDK4 as "a major catalytic subunit of mammalian D-type cyclins, which act during the G_1 phase of the cell cycle to enforce the decision of cells to enter the S phase. Said definition for CDK4 includes an

extremely large number of naturally-occurring known and unknown proteins as well as variant thereof; the specification fails to provide any structural limitations. Since Claims 1-3 and 5 recite a polypeptide that binds to any one of said extremely large number of "CDK-4 proteins", a person of ordinary skill in the art of would not know the metes and bounds of the recited invention. Claim 4, as dependent on Claim 3, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the same reasons.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

In this regard, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptide Tyr-Ser-Gly-Pro-Pro-Cys-Ser-Ser-Arg-Arg-Arg-Asn-Ser-Tyr-Glu, which binds to the CDK4 polypeptide used in Examples I-III, does not reasonably provide enablement for any polypeptide comprising any other peptide having the sequence Tyr-Ser-Gly-Pro-Pro-Xaa_1-Xaa_2-Xaa_3-Arg-Arg- Xaa_4-Asn- Xaa_5-Tyr- Xaa_6, wherein Xaa_1 is Cys or Ser, Xaa_2 is Ser or Gly, Xaa_3 is Ser, Ala, or Pro, Xaa_4 is Arg or Gln, Xaa_5 is Ser, Cys, or Gly, and Xaa_6 is Asp or Glu, wherein said polypeptide binds to any protein having any structure and having "CDK4 activity". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-5 are so broad as to encompass any polypeptide comprising any peptide having the sequence Tyr-Ser-Gly-Pro-Pro-Xaa_1-Xaa_2-Xaa_3-Arg-Arg- Xaa_4-Asn- Xaa_5-Tyr- Xaa_6, wherein Xaa_1 is Cys or Ser, Xaa_2 is Ser or Gly, Xaa_3 is Ser, Ala, or Pro, Xaa_4 is Arg or Gln, Xaa_5 is Ser, Cys, or Gly, and Xaa_6 is Asp or Glu, including Tyr-Ser-Gly-Pro-Pro-Ser-Gly-Ala-Arg-Arg-Arg-Asn-Cys-Tyr-Glu, wherein the polypeptide binds to any protein having "CDK4 activity". The scope of these claims is not commensurate with the enablement provided by the disclosure because one of skill in the art could not determine which of the recited polypeptides have "CDK4 binding activity" without undue experimentation in view of the extremely large number of "CDK4 proteins", as broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired "CDK4 binding activity" requires a knowledge of and guidance with regard to which amino acids in the

protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. Furthermore, to determine if a peptide binds to a protein with "CDK4 activity", the artisan must use a protein with "CDK4 activity". Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired "CDK4 activity" also requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. In view of the idenfiniteness and breath of the recited "CDK4 activity", the experimentation to test polypeptides for "CDK4 binding activity" would be undue because determining if the peptide had such activity would require many different assays using many different proteins with any "CDK4 activity". The disclosure fails to describe any said assay because the specification fails describe the use of any specific protein having any "CDK4 activity" that can be used to test for binding of the recited peptides.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Wishart et al, 1995; Witkowski et al, 1999). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 1-5 which, encompasses all polypeptides comprising any peptide having the sequence Tyr-Ser-Gly-Pro-Pro-Xaa_1-Xaa_2-Xaa_3-Arg-Arg- Xaa_4-Asn- Xaa_5-Tyr- Xaa_6, wherein Xaa_1 is Cys or Ser, Xaa_2 is Ser or Gly, Xaa_3 is Ser, Ala, or Pro, Xaa_4 is Arg or Gln, Xaa_5 is Ser, Cys, or Gly, and Xaa_6 is Asp or Glu, wherein the polypeptide binds to any protein having "CDK4 activity". The specification does not support the broad scope of Claims 1-5 because the specification does not establish: (A) any assay using a "CDK4 protein" of defined structure wherein the "CDK4" protein binds any of the recited peptides; (B) regions of the "CDK4" protein structure which may be modified without effecting the "CDK4 activity", wherein the "CDK4" protein can be used in an assay to test for binding of the recited peptides; (C) the general tolerance to structural modification for the "CDK4 activity" of any protein and the extent of such tolerance, wherein the protein can be used in an assay to test for binding of the recited peptides; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired "CDK4 activity", wherein the protein can be used in an assay to test for binding of the recited peptides; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices of proteins is likely to have "CDK4 activity" and can be used in an assay to test for binding of the recited peptides.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polypeptides comprising any peptide having the sequence Tyr-Ser-Gly-Pro-Pro-Xaa_1-Xaa_2-Xaa_3-Arg-Arg- Xaa_4-Asn- Xaa_5-Tyr- Xaa_6, wherein Xaa_1 is Cys or Ser, Xaa_2 is Ser or Gly, Xaa_3 is Ser, Ala, or Pro, Xaa_4 is Arg or Gln, Xaa_5 is Ser, Cys, or Gly, and Xaa_6 is Asp or Glu, including Tyr-Ser-Gly-Pro-Pro-Ser-Gly-Ala-Arg-Arg-Arg-

Asn-Cys-Tyr-Glu, wherein the polypeptide binds to any protein having "CDK4 activity" . The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of polypeptides that bind to any "CDK4" protein. The specification teaches the structure of only a single representative species of such polypeptides. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of having the sequence Tyr-Ser-Gly-Pro-Pro-Xaa_1-Xaa_2-Xaa_3-Arg-Arg- Xaa_4-Asn- Xaa_5-Tyr- Xaa_6, wherein Xaa_1 is Cys or Ser, Xaa_2 is Ser or Gly, Xaa_3 is Ser, Ala, or Pro, Xaa_4 is Arg or Gln, Xaa_5 is Ser, Cys, or Gly, and Xaa_6 is Asp or Glu, wherein the polypeptide binds to any protein having "CDK4 activity". Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to polypeptides that have the function of binding to a genus of proteins having "CDK4 activity". The specification teaches the structure of no proteins having said "CDK4 activity" and that bind the recited polypeptides. Moreover, the specification fails to describe any representative species of said "CDK4 protein" by any identifying characteristics or properties other than the functionality of being a protein that acts during the G_1 phase of the cell cycle to enforce the decision of cells to enter the S phase. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

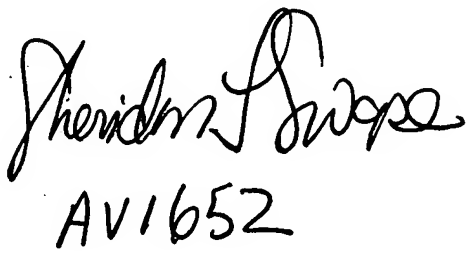
Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Pearson-White et al, 1991. Pearson-White et al teach a polynucleotide that encodes a polypeptide, human myoD, comprising residues 1-15 of SEQ ID NO: 3. Therefore, Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Pearson-White et al, 1991.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Sheridan Lee Swope, Ph.D.



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